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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/071,585	02/08/2002	Marek Kwiatkowski	11989-008001	2835
26191	7590	10/05/2007		
FISH & RICHARDSON P.C. PO BOX 1022 MINNEAPOLIS, MN 55440-1022			EXAMINER LU, FRANK WEI MIN	
			ART UNIT 1634	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/071,585	Applicant(s) KWIATKOWSKI, MAREK	
	Examiner Frank W Lu	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 November 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-29 and 32-35 is/are pending in the application.
- 4a) Of the above claim(s) 4,5,10-13,18,20-23,29,32 and 33 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,17,19,24,26-28,34 and 35 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 08 February 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Amendment

1. Applicant's response to the office action filed on July 18, 2007 has been entered. The claims pending in this application are claims 1-29 and 32-35 wherein claims 4, 5, 10-13, 18, 20-23, 29, 32, and 33 have been withdrawn due to species election. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn in view of amendment filed on July 18, 2007.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. New Matter

Claims 27, 28, and 35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The recitation "said first separation tag interacts more strongly than said second separation tag with said separation medium" is added to the newly amended independent claim 27. Although the specification describes that "[A] mixture of bifunctional and non-bifunctional oligonucleotides can be contacted with an appropriate separation medium that retains

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bifunctional oligonucleotides as well as non-bifunctional oligonucleotides containing the separation tag that interacts more strongly with the separation medium" (see page 11, last paragraph), page 11, lines 16-29 and page 17, line 18 to page 18, line 12 of the specification suggested by applicant fail to define or provide any disclosure to support such claim recitation.

MPEP 2163.06 notes "If NEW MATTER IS ADDED TO THE CLAIMS, THE EXAMINER SHOULD REJECT THE CLAIMS UNDER 35 U.S.C. 112, FIRST PARAGRAPH - WRITTEN DESCRIPTION REQUIREMENT. *IN RE RASMUSSEN*, 650 F.2D 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application". MPEP 2163.06 further notes "WHEN AN AMENDMENT IS FILED IN REPLY TO AN OBJECTION OR REJECTION BASED ON 35 U.S.C. 112, FIRST PARAGRAPH, A STUDY OF THE ENTIRE APPLICATION IS OFTEN NECESSARY TO DETERMINE WHETHER OR NOT "NEW MATTER" IS INVOLVED. *APPLICANT SHOULD THEREFORE SPECIFICALLY POINT OUT THE SUPPORT FOR ANY AMENDMENTS MADE TO THE DISCLOSURE*" (emphasis added).

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-3, 6-9, 14-17, 19, 24-29, 34, and 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
6. Claim 1 or 27 is rejected as vague and indefinite. Although claim 1 or 27 is directed to a method for separating oligonucleotide, from the claim, it is unclear whether bifunctional oligonucleotides are separated from non-bifunctional oligonucleotides or not. Please clarify.
7. Claim 1 is rejected as vague and indefinite in view of step c) because it is unclear that at least one non-bifunctional oligonucleotide is eluted from where. Please clarify.

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8. Claim 26 is rejected as vague and indefinite in view of step e) because it is unclear that a non-bifunctional oligonucleotide is eluted from where. Please clarify.
9. Claim 27 is rejected as vague and indefinite in view of steps c) and e) because it is unclear that non-bifunctional oligonucleotides are eluted from where. Please clarify.
10. Claim 34 recites the limitation "the non-cleaved said first separation tag or said second separation tag" in the claim. There is insufficient antecedent basis for this limitation in the claim because there is no phrase "non-cleaved said first separation tag or said second separation tag" in claim 26. Please clarify.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(c) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. Claims 1, 7-9, 14, 17, and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Blocker *et al.*, (US Patent No.4, 997,927, published on March 5,1991).

Regarding claims 1 and 7, Blocker *et al.*, teach providing a plurality of oligonucleotides, said plurality of oligonucleotides (ie., crude synthesized oligonucleotides) comprising at least one bifunctional oligonucleotide (ie., synthesized oligonucleotides with a trityl group at the 5'

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end) and at least one non-bifunctional oligonucleotide (ie., synthesized oligonucleotides without a trityl group at its 5' end) wherein each said at least one bifunctional oligonucleotide comprises a first separation tag (ie., a trityl group at its 5' end) attached to a first end of said at least one bifunctional oligonucleotide and a second separation tag (ie., the hydroxyl group on the 3' terminal nucleotide) attached to a second end of said at least one bifunctional oligonucleotide, wherein said at least one non-bifunctional oligonucleotide lacks either (ie., trityl group at the 5' end) or both of said first and second separation tags, and wherein cleavage of a separation tags (ie., the hydroxyl group on the 3' terminal nucleotide by removing the 3' terminal nucleotide) yields an oligonucleotide having a 3' hydroxyl moiety, contacting said plurality of oligonucleotides with a separation medium (ie., DEAE column) under conditions effective for adhering said at least one bifunctional oligonucleotide and at least one non-bifunctional oligonucleotide to said separation medium, and selectively eluting at least one non-bifunctional oligonucleotide (ie., synthesized oligonucleotides without a trityl group at its 5' end) as recited in claim 1 wherein said first and said second separation tags are different as recited in claim 7 (see column 2, lines 29-65, claim 1 in column 5, and Figure 1).

Regarding claims 8 and 9, Blocker *et al.*, teach that either of said first or said second separation tags comprise a separation unit selected from the group consisting of alkoxytrityl, alkoxypixyl, alkylthioformacetal, methylthioalkyl, derivatives of mercaptodimethoxytrityl or mercaptotrityl, and a hydrocarbon chain introduced in a form of a linear or branched diol, and combinations thereof as recited in claim 8 wherein said alkoxytrityl is selected from the group consisting of decyloxymethoxy trityl (C10Tr), 4-hyloxymethoxytrityl (C6Tr), dimethoxytrityl (DMTr), and monomethoxytrityl (MMTr) as recited in claim 9 (see column 4, lines 47-67).

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Regarding claim 14, Blocker *et al.*, teach that a cleavable unit of either of said first or said second separation tags is selected from the group consisting of acid labile (ie., trityl that can be cleaved by acid), fluoride ion labile, photolabile, redox labile, and electrophilic labile moieties (see column 2, lines 52-67).

Regarding claim 17, Blocker *et al.*, teach that said separation medium is ion exchange separation media (ie., DEAE column) as recited in claim 17 (see column 2, lines 43-51).

Regarding claim 24, Blocker *et al.*, teach further comprises eluting said at least one bifunctional oligonucleotide (ie., synthesized oligonucleotides without a trityl group at the 5' end) (see column 2, lines 29-65, claim 1 in column 5, and Figure 1).

Therefore, Blocker *et al.*, teach all limitations recited in claims 1, 7-9, 14, 17, and 24.

Response to Arguments

In page 12 of applicant's remarks, applicant argues that "[T]he Blocker *et al.* patent does not disclose all elements of independent claim 1, and thus does not anticipate the present claims. For example, like the Bonora *et al.* reference, the Blocker *et al.* patent fails to disclose bifunctional nucleotides as recited in the present claims. Again, Applicant's specification discloses that a separation tag is a chemical group or moiety bonded to either the 3' or 5' end of an oligonucleotide that allows an oligonucleotide having the separation tag to be separated from other oligonucleotides that lack the separation tag, that a cleavable unit of a 3' separation tag can be attached to the 3' oxygen of the first nucleotide in the oligomer, that suitable cleavable units on the 3' end of an oligonucleotide regenerate a free 3' OH after being cleaved, and that disiloxy groups, alkyl thiomethyl and hydrocarbyldithiomethyl groups, photolabile groups, redox active groups, and electrophilic reagents are examples of suitable cleavable units that can be

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components of a linker. Thus, it is clear that a hydroxyl group at the 3' end is not considered a separation tag. Further, present claim 1 recites that cleavage of either the first separation tag or the second separation tag yields an oligonucleotide having a 3' hydroxyl moiety. It is clear that cleavage of a 3' hydroxyl group would not yield an oligonucleotide having a 3' hydroxyl moiety. Thus, the Examiner's assertions that a hydroxyl group at the 3' of an oligonucleotide is equivalent to a separation tag are incorrect. For at least these reasons, the Blocker *et al.* patent does not anticipate the present claims".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, a hydroxyl group at the 3' end can be used a separation tag because the hydroxyl group at the 3' end of an oligonucleotide is a chemical group and can be used to separate an oligonucleotide with a hydroxyl group at its 3' end from an oligonucleotide without a hydroxyl group at its 3' end. Second, cleavage of a 3' hydroxyl group can yield an oligonucleotide having a 3' hydroxyl moiety by removing the 3' terminal nucleotide of an oligonucleotide.

13. Claims 1, 2, 14, 17, and 24 are rejected under 35 U.S.C. 102(e) as being anticipated by Pieken *et al.*, (US Patent No. 7,098,326, priority date: January 23, 2002).

Regarding claims 1 and 7, Pieken *et al.*, teach providing a plurality of oligonucleotides, said plurality of oligonucleotides (ie., crude synthesized oligonucleotides) comprising at least one bifunctional oligonucleotide (ie., synthesized full length oligonucleotides with a DMT group at its 5' end) and at least one non-bifunctional oligonucleotide (ie., synthesized truncated oligonucleotides without a DMT group at its 5' end) wherein each said at least one bifunctional

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oligonucleotide comprises a first separation tag (ie., a DMT group at the 5' end) attached to a first end of said at least one bifunctional oligonucleotide and a second separation tag (ie., the hydroxyl group on the 3' terminal nucleotide) attached to a second end of said at least one bifunctional oligonucleotide, wherein said at least one non-bifunctional oligonucleotide lacks either (ie., a DMT group at the 5' end) or both of said first and second separation tags, and wherein cleavage of a separation tags (ie., the hydroxyl group on the 3' terminal nucleotide by removing the 3' terminal nucleotide) yields an oligonucleotide having a 3' hydroxyl moiety, contacting said plurality of oligonucleotides with a separation medium (ie., the anion-exchange HPLC) under conditions effective for adhering said at least one bifunctional oligonucleotide and at least one non-bifunctional oligonucleotide to said separation medium, and selectively eluting at least one non-bifunctional oligonucleotide (ie., synthesized oligonucleotides without a DMT group at the 5' end) as recited in claim 1 wherein said non-bifunctional oligonucleotide comprises truncated oligonucleotides as recited in claim 2 and said first and said second separation tags are different as recited in claim 7 (see abstract, columns 4-6, and Figures 1, 2, 5, and 6).

Regarding claim 17, Pieken *et al.*, teach that said separation medium is ion exchange separation media (ie., the anion-exchange HPLC) as recited in claim 17 (see Figures 5 and 6).

Regarding claim 24, Pieken *et al.*, teach further comprises eluting said at least one bifunctional oligonucleotide (ie., synthesized truncated oligonucleotides without a DMT group at its 5' end) (see Figures 5 and 6).

Therefore, Pieken *et al.*, teach all limitations recited in claims 1, 2, 7, 17, and 24.

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Conclusion

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. No claim is allowed.

16. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571)272-0735.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

September 26, 2007

A handwritten signature in black ink, appearing to read 'Frank Lu', is positioned above the printed name.

FRANK LU
PRIMARY EXAMINER